(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 29 September 2005 (29.09.2005)

PCT

(10) International Publication Number WO 2005/090348 A1

(51) International Patent Classification⁷: C07D 471/04, A61K 31/437, A61P 29/00

(21) International Application Number:

PCT/GB2005/000983

(22) International Filing Date: 15 March 2005 (15.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0405933.3 16 March 2004 (16.03.2004) GB

(71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ALLEN, David, George [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). COE, Diane, Mary [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). COOK, Caroline, Mary [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

DOWLE, Michael, Dennis [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). EDLIN, Christopher, David [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). HAMBLIN, Julie, Nicole [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). JOHNSON, Martin, Redpath [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **JONES**, Paul, Spencer [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). LINDVALL, Mika, Kristian [FI/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). MITCHELL, Charlotte, Jane [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). REDGRAVE, Alison, Judith [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). TRIVEDI, Naimisha [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

(74) Agent: BREEN, Anthony, Paul; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

[Continued on next page]

(54) Title: PYRAZOLO '3,4-B! PYRIDINE COMPOUNDS, AND THEIR USE AS PHOSPHODIESTERASE TYPE 4 (PDE4) INHIBITORS

(57) Abstract: The invention provides a compound of formula (I) or a salt thereof: formula (I) wherein W is Ar, $-CR^4R^5Ar$ or a group (y) or (y1), wherein Ar is (x) or (z): formulae (x), (z), (y), (y1) R^1 is C_{1-4} alkyl, C_{1-3} fluoroalkyl or CH_2CH_2OH . R^2 is C_{2-6} alkyl, C_{3-6} cycloalkyl or $-(CH_2)_n^4$ - C_{3-6} cycloalkyl; and R^3 is optionally substituted C_{3-8} cycloalkyl, optionally substituted mono unsaturated C_{5-7} cycloalkenyl, an optionally substituted heterocyclic group (aa), (bb) or (cc) (in which Y is O, S, SO₂, or R^{10}), or a bicyclic group (ee): formulae (aa), (bb), (cc), (ee). The invention also relates to the use of the compounds in therapy as inhibitors of phosphodiesterase type IV (PDE4), and/or for the treatment and/or prophylaxis of inflammatory and/or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis or allergic rhinitis.

WO 2005/090348 A1

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.